Complete Summary

GUIDELINE TITLE

Use of anthrax vaccine in the United States. Recommendations of the Advisory Committee on Immunization Practices.

BIBLIOGRAPHIC SOURCE(S)

Use of anthrax vaccine in the United States. Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2000 Dec 15;49(RR-15):1-21. [87 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Anthrax

GUIDELINE CATEGORY

Prevention

CLINICAL SPECIALTY

Infectious Diseases
Internal Medicine
Preventive Medicine

INTENDED USERS

Other
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

- To review the use of aluminum hydroxide adsorbed cell-free anthrax vaccine in the United States for protection against disease caused by Bacillus anthracis.
- To review information on the use of chemoprophylaxis against Bacillus anthracis.

TARGET POPULATION

Individuals residing in the United States exposed to Bacillus anthracis, including:

- Individuals who may come in contact with an infected animal or animal products (e.g., wool, hair, or hides).
- Individuals with possible occupational or laboratory exposure to Bacillus anthracis.
- Military and other select populations who may be at risk for exposure to Bacillus anthracis.

INTERVENTIONS AND PRACTICES CONSIDERED

1. Vaccination with aluminum hydroxide adsorbed cell-free anthrax vaccine (Anthrax Vaccine Adsorbed [AVA], marketed by BioPort Corporation).
2. Post-exposure antibiotic prophylaxis:
    - Oral fluoroquinolones (ciprofloxacin, ofloxacin)
    - Oral tetracyclines (doxycycline)
    - Oral penicillins (penicillin VK, amoxicillin)

MAJOR OUTCOMES CONSIDERED

- Vaccine immunogenicity and efficacy
- Incidence and progression of disease after exposure to aerosolized anthrax
- Vaccination-related adverse events

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Not stated

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Excerpted by the National Guideline Clearinghouse (NGC)

Recommended Vaccination Schedule

Primary vaccination consists of three subcutaneous injections at 0, 2, and 4 weeks, and three booster vaccinations at 6, 12, and 18 months. To maintain immunity, the manufacturer recommends an annual booster injection.

Preexposure Vaccination

Occupational and Laboratory Exposures

Routine vaccination with Anthrax Vaccine Adsorbed (AVA) is indicated for persons engaged in:

a. Work involving production quantities or concentrations of Bacillus anthracis cultures
b. Activities with a high potential for aerosol production

Laboratorians using standard Biosafety Level 2 practices in the routine processing of clinical samples are not at increased risk for exposure to Bacillus anthracis spores.

The risk for persons who come in contact in the workplace with imported animal hides, furs, bone meal, wool, animal hair, or bristles has been reduced by changes in industry standards and import restrictions. Routine preexposure vaccination is recommended only for persons in this group for whom these standards and restrictions are insufficient to prevent exposure to anthrax spores.

Routine vaccination of veterinarians in the United States is not recommended because of the low incidence of animal cases. However, vaccination might be indicated for veterinarians and other high-risk persons handling potentially infected animals in areas with a high incidence of anthrax cases.

Bioterrorism Preparedness

Although groups initially considered for preexposure vaccination for bioterrorism preparedness included emergency first responders, federal responders, medical practitioners, and private citizens, vaccination of these groups is not recommended. Recommendations regarding preexposure vaccination should be based on a calculable risk assessment. At present, the target population for a bioterrorist release of Bacillus anthracis cannot be predetermined, and the risk of exposure cannot be calculated. In addition, studies suggest an extremely low risk for exposure related to secondary aerosolization of previously settled Bacillus anthracis spores. Because of these factors, preexposure vaccination for the above groups is not recommended. For the military and other select populations or for groups for which a calculable risk can be assessed, preexposure vaccination may be indicated.

Options other than preexposure vaccination are available to protect personnel working in an area of a known previous release of Bacillus anthracis. If concern exists that persons entering an area of a previous release might be at risk for exposure from a re-release of a primary aerosol of the organism or exposure from a high concentration of settled spores in a specific area, initiation of prophylaxis should be considered with antibiotics alone or in combination with vaccine as is outlined in the section below on postexposure prophylaxis.

Postexposure Prophylaxis - Chemoprophylaxis and Vaccination

Penicillin and doxycycline are approved by Food and Drug Administration (FDA) for the treatment of anthrax and are considered the drugs of choice for the

treatment of naturally occurring anthrax. In addition, ciprofloxacin and ofloxacin have also demonstrated in vitro activity against Bacillus anthracis. On the basis of studies that demonstrated the effectiveness of ciprofloxacin in reducing the incidence and progression of inhalation anthrax in animal models, the Food and Drug Administration (FDA) recently approved the use of ciprofloxacin following aerosol exposure to Bacillus anthracis spores to prevent development or progression of inhalation anthrax in humans. Although naturally occurring Bacillus anthracis resistance to penicillin is rare, such resistance has been reported. As of November 2000, no naturally occurring resistance to tetracyclines or ciprofloxacin had been reported.

Antibiotics are effective against the germinated form of Bacillus anthracis but are not effective against the spore form of the organism. Following inhalation exposure, spores can survive in tissues for months without germination in nonhuman primates. This phenomenon of delayed vegetation of spores resulting in prolonged incubation periods has not been observed for routes of infection other than inhalation.

Currently, ciprofloxacin is the only antibiotic approved by the Food and Drug Administration (FDA) for use in reducing the incidence or progression of disease after exposure to aerosolized Bacillus anthracis. Although postexposure chemoprophylaxis using antibiotics alone has been effective in animal models, the definitive length of treatment is unclear. Several studies have demonstrated that short courses (5-10 days) of postexposure antibiotic therapy are not effective at preventing disease when large numbers of spores are inhaled. Longer courses of antibiotics may be effective.

Studies have demonstrated that antibiotics in combination with postexposure vaccination are effective at preventing disease in nonhuman primates after exposure to Bacillus anthracis spores. Vaccination alone after exposure was not protective. Because the current vaccine is labeled for use in specifically defined preexposure situations only, no Food and Drug Administration (FDA)-approved labeling addresses the optimal number of vaccinations for postexposure prophylaxis use of the vaccine. An estimated 83% of human vaccinees develop a vaccine-induced immune response after two doses of the vaccine and >95% develop a fourfold rise in antibody titer after three doses. Although the precise correlation between antibody titer and protection against disease is not clear, these studies of postexposure vaccine regimens used in combination with antibiotics in nonhuman primates have consistently documented that two to three doses of vaccine were sufficient to prevent development of disease once antibiotics were discontinued.

Only one study has directly compared antibiotics plus vaccine with a longer course of antibiotics following aerosol exposure. This study documented no significant difference in survival for animals treated with doxycycline alone for 30 days or animals treated with 30 days of doxycycline plus two doses of anthrax vaccine postexposure (nine of 10 versus nine of nine, $p = 0.4$). However, the study suggests a possible benefit of postexposure combination of antibiotics with vaccination.

Following Inhalation Exposure

Postexposure prophylaxis against Bacillus anthracis is recommended following an aerosol exposure to Bacillus anthracis spores. Such exposure might occur following an inadvertent exposure in the laboratory setting or a biological terrorist incident. Aerosol exposure is unlikely in settings outside a laboratory working with large volumes of Bacillus anthracis, textile mills working with heavily contaminated animal products, or following a biological terrorism or warfare attack. Following naturally occurring anthrax among livestock, cutaneous and rare gastrointestinal exposures among humans are possible, but inhalation anthrax has not been reported. Because of the potential persistence of spores following a possible aerosol exposure, antibiotic therapy should be continued for at least 30 days if used alone, and although supporting data are less definitive, longer antibiotic therapy (up to 42-60 days) might be indicated. If the vaccine is available, antibiotics can be discontinued after three doses of vaccine have been administered according to the standard schedule (0, 2, and 4 weeks) (see Table 3 of the original guideline document for a list of suggested postexposure antibiotics and the corresponding dosing information for adults and children). Because of concern about the possible antibiotic resistance of Bacillus anthracis used in a bioterrorist attack, doxycycline or ciprofloxacin can be chosen initially for antibiotic chemoprophylaxis until organism susceptibilities are known. Antibiotic chemoprophylaxis can be switched to penicillin VK or amoxicillin once antibiotic susceptibilities are known and the organism is found to be penicillin susceptible with minimum inhibitory concentrations (MICs) attainable with oral therapy.

Although the shortened vaccine regimen has been effective when used in a postexposure regimen that includes antibiotics, the duration of protection from vaccination is not known. Therefore, if subsequent exposures occur, additional vaccinations might be required.

Following Cutaneous or Gastrointestinal Exposure

No controlled studies have been conducted in animals or humans to evaluate the use of antibiotics alone or in combination with vaccination following cutaneous or gastrointestinal exposure to Bacillus anthracis. Cutaneous and rare gastrointestinal exposures of humans are possible following outbreaks of anthrax in livestock. In these situations, on the basis of pathophysiology, reported incubation periods, current expert clinical judgment, and lack of data, postexposure prophylaxis might consist of antibiotic therapy for 7-14 days. Antibiotics could include any of those mentioned above and in Table 3 of the original guideline document.

Vaccination during Pregnancy

No studies have been published regarding use of anthrax vaccine among pregnant women. Pregnant women should be vaccinated against anthrax only if the potential benefits of vaccination outweigh the potential risks to the fetus.

Vaccination during Lactation

No data suggest increased risk for side effects or temporally related adverse events associated with receipt of anthrax vaccine by breast-feeding women or breast-fed children. Administration of nonlive vaccines (e.g., anthrax vaccine) during breast-feeding is not medically contraindicated.

Allergies

Although anaphylaxis following anthrax vaccination is extremely rare and no anaphylaxis deaths associated with Anthrax Vaccine Adsorbed (AVA) have been reported, this adverse event can be life threatening. Anthrax Vaccine Adsorbed (AVA) is contraindicated for persons who have experienced an anaphylactic reaction following a previous dose of Anthrax Vaccine Adsorbed (AVA) or any of the vaccine components.

Previous History of Anthrax Infection

Anthrax vaccine is contraindicated in persons who have recovered from anthrax because of previous observations of more severe adverse events among recipients with a vaccine history of anthrax than among nonrecipients.

Illness

In the context of the routine preexposure program, vaccination of persons with moderate or severe acute illness should be postponed until recovery. This prevents superimposing the adverse effects of the vaccine on the underlying illness or mistakenly attributing a manifestation of the underlying illness to the vaccine. Vaccine can be administered to persons who have mild illnesses with or without low-grade fever.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of evidence is not specifically stated for each recommendation.

The efficacy of Anthrax Vaccine Adsorbed (AVA) is based on several studies in animals, on controlled vaccine trial in humans, and immunogenicity data for both humans and lower mammalian species.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Preexposure vaccination

Protection of individuals who are at high-risk for coming in contact with Bacillus anthracis.

Postexposure prophylaxis

Studies have demonstrated that antibiotics in combination with postexposure vaccination are effective at preventing disease in nonhuman primates after exposure to Bacillus anthracis spores.

POTENTIAL HARMS

Anthrax vaccination:

- Prelicensure Adverse Event Surveillance
    - Local Reactions: In Anthrax Vaccine Adsorbed (AVA) prelicensure evaluations, severe local reactions (defined as edema or induration >120 mm) occurred after 1% of vaccinations. Moderate local reactions (defined as edema and induration of 30 mm-120 mm) occurred after 3% of vaccinations. Mild local reactions (defined as erythema, edema, and induration <30 mm) occurred after 20% of vaccinations.
    - Systemic Reactions: In Anthrax Vaccine Adsorbed (AVA) prelicensure evaluations, systemic reactions (i.e., fever, chills, body aches, or nausea) occurred in <0.06% (in four of approximately 7,000) of vaccine recipients.
- Postlicensure Adverse Event Surveillance
    - Data regarding potential adverse events following anthrax vaccination are available from the Vaccine Adverse Event Reporting System (VAERS). From January 1, 1990, through August 31, 2000, at least 1,859,000 doses of anthrax vaccine were distributed in the United States. During this period, Vaccine Adverse Event Reporting System (VAERS) received 1,544 reports of adverse events; of these, 76 (5%) were serious. A serious event is one that results in death, hospitalization, or permanent disability or is life-threatening. Approximately 75% of the reports were for persons aged <40 years; 25% were female, and 89% received anthrax vaccine alone. The most frequently reported adverse events were injection-site hypersensitivity, injection-site edema, injection-site pain, headache, arthralgia, asthenia, and pruritis. Two reports of anaphylaxis have been received.
    - Serious adverse events infrequently reported (<10) to Vaccine Adverse Event Reporting System have included cellulitis, pneumonia, Guillain-Barré syndrome, seizures, cardiomyopathy, systemic lupus erythematosus, multiple sclerosis, collagen vascular disease, sepsis, angioedema, and transverse myelitis. Analysis of Vaccine Adverse Event Reporting System data documented no pattern of serious adverse events clearly associated with the vaccine, except injection-site reactions. Because of the limitations of spontaneous reporting systems, determining causality for specific types of adverse events, with the exception of injection-site reactions, is often not possible using Vaccine Adverse Event Reporting System data alone.

Note: See the original guideline document for a detailed discussion of adverse events associated with the use of Anthrax Vaccine Adsorbed (AVA) derived from published studies.

Antibiotic prophylaxis:

- Although naturally occurring Bacillus anthracis resistance to penicillin is rare, such resistance has been reported.

Subgroups Most Likely to be Harmed:

- Patients experiencing an anaphylactic reaction following a previous dose of Anthrax Vaccine Adsorbed (AVA) or any of the vaccine components.
- Patients with a previous history of anthrax infection.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- No data are available regarding the efficacy of anthrax vaccine for persons aged <18 years and >65 years.
- The basis for the schedule of vaccinations at 0, 2, and 4 weeks, and 6, 12, and 18 months followed by annual boosters is not well defined.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Staying Healthy

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Use of anthrax vaccine in the United States. Recommendations of the Advisory Committee on Immunization Practices. MMWR Recomm Rep 2000 Dec 15;49(RR-15):1-21. [87 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2000 Dec 15

GUIDELINE DEVELOPER(S)

Centers for Disease Control and Prevention - Federal Government Agency [U.S.]

SOURCE(S) OF FUNDING

United States Government

GUIDELINE COMMITTEE

Advisory Committee on Immunization Practices

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Advisory Committee on Immunization Practices Membership List, October 2000: John F. Modlin, M.D., Chairman; Dixie E. Snider, Jr., M.D., M.P.H., Executive Secretary; Dennis A. Brooks, M.D., M.P.H.; Richard D. Clover, M.D.; Fernando A. Guerra, M.D.; Charles M. Helms, M.D., Ph.D.; David R. Johnson, M.D., M.P.H.; Chinh T. Le, M.D.; Paul A. Offit, M.D.; Margaret B. Rennels, M.D.; Lucy S. Tompkins, M.D., Ph.D.; Bonnie M. Word, M.D.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

An update is not in progress at this time.

GUIDELINE AVAILABILITY

Electronic copies: Available from the Centers for Disease Control and Prevention (CDC) Web site.

Also available (in Portable Document Format (PDF) from the Centers for Disease Control and Prevention (CDC) Web site, Centers for Disease Control and Prevention (CDC) Web site.

Print copies: Available from CDC, MMWR MS (C-08), Atlanta, GA 30333. Additional copies can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9325; (202) 783-3238.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on March 15, 2001.

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